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Hulkkonen, Sina

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by [Hulkkonen S](#), [Shiri R](#), [Auvinen J](#), [Miettunen J](#), [Karppinen J](#), [Ryhänen J](#)

To date, few prospective cohort studies on occupational risk factors for CTS have examined the general working population. Our prospective cohort study of a large birth cohort (N=6326) aged 31 at baseline found that excess body mass and occupational physical factors increase the risk of hospitalization for CTS. Excess body mass potentiates the adverse effects of strenuous work on CTS.

Affiliation: Department of Hand Surgery, Helsinki University Hospital and University of Helsinki, PO Box 266, FI-00029 HUS, Finland. sina.hulkkonen@gmail.com

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Risk factors of hospitalization for carpal tunnel syndrome among the general working population

by Sina Hulkkonen, MD,¹ Rahman Shiri, MD, PhD,² Juha Auvinen, MD, PhD,^{3,4,5} Jouko Miettunen, PhD,^{3,4} Jaro Karppinen, MD, PhD,^{4,6} Jorma Ryhänen, MD, PhD¹

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Objectives Carpal tunnel syndrome (CTS) causes a considerable amount of sick leave and healthcare costs. The etiology of CTS is multifactorial, involving both personal and occupational risk factors. To date, few prospective cohort studies on occupational risk factors of CTS have examined the general working population.

Methods The study population consisted of participants from the Northern Finland Birth Cohort of 1966 who attended the 31-year follow-up in 1997 and were working ≥ 3 days a week in a paid job (N=6326). Information on socio-economic status, weight and height, smoking, exposure to occupational physical factors, and long-term illnesses was collected at baseline in 1997. Data on hospitalizations due to CTS came from the Care Register for Health Care, 1997–2016.

Results Between 1997 and 2016, 3.4% of the participants had been hospitalized (attended secondary care) for CTS. After adjusting for confounders, women [hazard ratio (HR) 3.77, 95% confidence interval (CI) 2.70–5.25], overweight/obese participants (HR 1.69, 95% CI 1.29–2.22), smokers (HR 1.48, 95% CI 1.12–1.96), farmers and manual workers (HR 3.02, 95% CI 1.85–4.92 compared with upper clerical workers), lower clerical workers (HR 1.74, 95% CI=1.08–2.80), workers exposed to hand vibration (HR 2.29, 95% CI 1.48–3.54) and participants with physically demanding jobs (HR 1.71, CI 1.06–2.76) were at increased risk of hospitalization for CTS. Physically demanding work increased the risk of hospitalization for CTS for overweight/obese participants at baseline, but not for participants of normal weight.

Conclusions Excess body mass and occupational physical factors increase the risk of hospitalization for CTS. Excess body mass potentiates the adverse effects of strenuous work on CTS.

Key terms cohort study; median nerve; musculoskeletal disorder; occupational exposure; overweight.

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper extremities, with an incidence rate of 3.3–3.5 per 1000 person-years and a prevalence of 1–5% in the general population (1–4). CTS can cause pain, numbness and loss of hand function in the affected hand. Of all musculoskeletal problems occurring in the working population, CTS causes a considerable amount of sick leave and healthcare costs (5–8).

The etiology of CTS is considered multifactorial, and involves both personal and occupational risk fac-

tors. Female gender, obesity (9), diabetes (10) rheumatoid arthritis (11), hypothyroidism (12), and smoking (13) have previously been recognized as risk factors. The prevalence of CTS varies from 0.6–61% in different working populations (14). In studies conducted in specific occupational groups, high force gripping (15), lifting heavy objects, exposure to vibration to hands, and repetitive wrist movements (16–19) were associated with increased risk for CTS. To date, only a limited number of prospective cohort studies of occupational

¹ Department of Hand Surgery, Helsinki University Hospital and University of Helsinki, Finland.

² Finnish Institute of Occupational Health, Helsinki, Finland.

³ Center for Life Course Health Research, University of Oulu, Oulu, Finland.

⁴ Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland.

⁵ Oulunkaari Health Center, Ii, Finland.

⁶ Finnish Institute of Occupational Health, Oulu, Finland.

Correspondence to: Sina Hulkkonen, Department of Hand Surgery, Helsinki University Hospital and University of Helsinki, PO Box 266, FI-00029 HUS, Finland. [E-mail: sina.hulkkonen@gmail.com]

risk factors of CTS have been conducted among the general working population (3, 20).

Knowledge of CTS risk factors is essential for preventing the condition. The aim of the current study was to determine the effects of personal factors and exposure to occupational physical workload factors on hospitalization for CTS in the general population.

Methods

Study population

The study population consisted of the Northern Finland Birth Cohort of 1966 (NFBC1966). Originally, 12 231 participants with an expected date of birth in 1966 were born in the cohort in the Oulu and Lapland provinces (21). A total of 8719 individuals participated in the 31-year follow-up study in 1997 and signed their informed consent to voluntarily participate in the study. Of these, 16 participants were diagnosed with CTS before the 31-year follow-up and were excluded from the analyses. Of the remaining 8703 participants, we only included those who were working ≥ 3 days a week in a paid job and answered the postal questionnaire on work-related factors (N=6326). The subsample consisted of 3824 participants who answered additional work-related questions in a questionnaire conducted during the clinical examination. In both the total sample and the subsample, we only included participants with no missing data (figure 1).

The participants' personal identification numbers were replaced with study identification codes. The Ethics Committee of the Northern Ostrobothnia Hospital District approved the study (ETTMK: 107/2017), which followed the principles of the Declaration of Helsinki (as revised in 2008) of the World Medical Association.

Hospitalizations for carpal tunnel syndrome

The data on hospitalizations due to CTS were obtained from the Care Register for Health Care. This is a national register that covers both public and private hospitals in Finland (22). It contains information on patients' demographic features, diagnoses, surgical procedures, and dates of admission and discharge. The diagnoses are coded according to the International Classification of Diagnoses (ICD). CTS diagnosis was coded 357.2 according to the eighth revision of ICD, 1981–1986, 354.0 according to the ninth revision of ICD, 1987–1995, and G56.0 according to the tenth revision of ICD, 1996–2016. The diagnoses were obtained from hospital data, including both out- and inpatient-based services and specialist care, with CTS as the primary diagnosis.

Study population at baseline

The cohort population was examined at 31 years in 1997. Data at 31 years was collected via postal questionnaire and during a clinical examination. In all, 6326 participants answered the questions on occupational risk factors in the postal questionnaire: "Are you

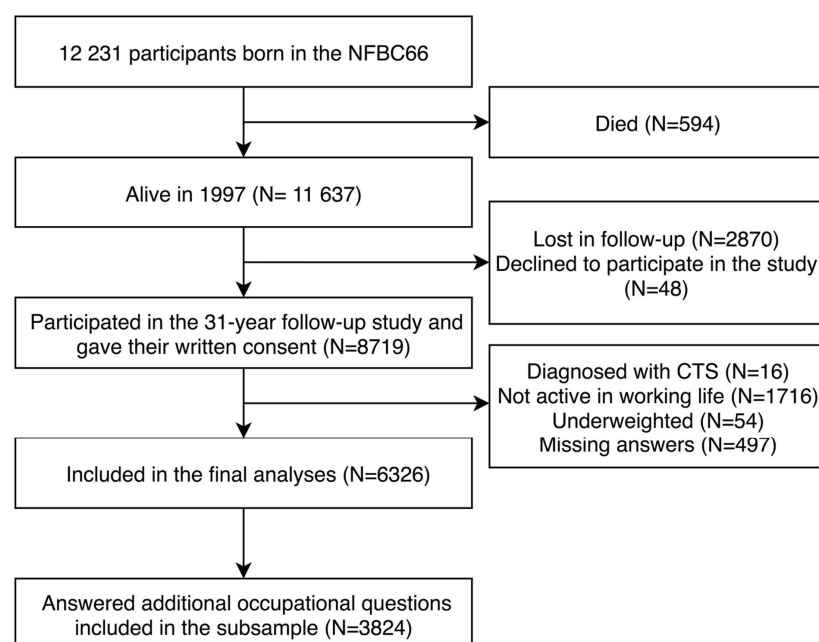


Figure 1. Flowchart of study population. [NFBC1966=the Northern Finland Birth Cohort of 1966.]

exposed to the following in your work?" The exposures were defined as: heat, cold, temperature changes, and vibration to hands. The participants who answered the additional occupational questions in the clinical examination formed the subsample ($N=3824$). The additional occupational questions were: "Do you encounter the following in your work?" with the definitions: heavy physical work, repetitive movements, lifting 1–15 kg objects, lifting >15 kg objects, and working with arms elevated above shoulder level. The answers to the postal questionnaire and additional questions on occupational exposure were divided into two categories: none/light, and moderate/heavy exposure.

According to Statistics Finland, socioeconomic status was defined by occupation and activity in working life with nine categories: farmers, entrepreneurs, clerical workers (lower and upper), manual workers, students, pensioners, the unemployed, and unknown (23). As we only included participants active in working life, the variable was divided into four categories: upper clerical workers, lower clerical workers, entrepreneurs, and farmers/manual workers (categories combined). Body mass index (BMI, kg/m^2) was calculated from height and weight measurements in the clinical examination or, if missing, from the height and weight information in the postal questionnaire. The variable was given two categories: normal ($18.5 \leq \text{BMI} < 25$) and overweight/obese ($\text{BMI} \geq 25$). A small number of individuals had $\text{BMI} < 18.5$ and were excluded from the analysis ($N=54$). We collected information on smoking history by the postal questionnaire. The participants were divided into two categories: never-smokers and smokers (including both previous and present regular smokers). Information on diabetes, rheumatoid arthritis, hypothyroidism and other illnesses were self-reported at 31-year follow-up (no/yes).

Statistical analysis

First, the associations of the background characteristics and occupational physical factors with hospitalization for CTS were assessed using the univariable Cox proportional hazards regression model. Second, all the variables that remained significant in the sex-specific analyses or in the both sexes combined analyses, and were controlled for sex were included in the multivariable Cox proportional hazards regression models. The five variables made up of additional occupational questions were analyzed in the subsample ($N=3824$). We ran the final models for the variables that remained statistically significant in the multivariable models. Moreover, we performed stratified analyses to determine whether overweight/obesity modifies the associations between occupational physical workload factors and hospitalization for CTS. A variable was considered significant if its

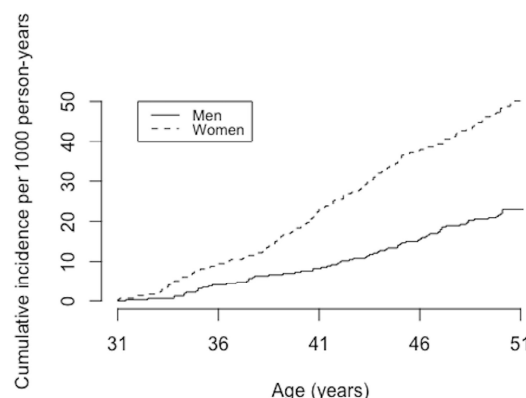


Figure 2. Cumulative incidence of hospital-diagnosed carpal tunnel syndrome (CTS) in study population during follow-up. Sixteen participants were diagnosed with CTS before the baseline of 31 years.

95% CI did not include 1. We also tested multiplicative interactions between gender and personal or occupational variables by adding gender X to the variable of interest in the multivariate models. Every variable of interest was tested separately. For the statistical analysis we used R version 3.4.4.

Results

At baseline, 23% of the study population were upper clerical workers, 35% lower clerical workers, 8% entrepreneurs and 34% farmers or manual workers; 40% were overweight or obese; and 49% were past or current smokers. Of the 6326 study participants, 77 had diabetes, 105 had thyroid disease and 53 had rheumatoid arthritis. The follow-up started in 1997 and ended in 2016 and the mean follow-up time was 18.3 [standard deviation (SD) 4.1] years. During the follow-up period, 215 participants (3.4%) were hospitalized due to CTS. The incidence of hospitalization for CTS was higher among women than men (figure 2). The incidence of hospitalization for CTS was 2.6 per 1000 person-years among women and 1.2 per 1000 person-years among men. The demographic features of the whole study sample and the study subsample were similar.

Socioeconomic status, smoking, a BMI of ≥ 25 , exposure to heat, temperature changes, and exposure to vibration to hands were associated with CTS in the analyses controlled for sex. Diabetes, thyroid diseases and rheumatoid arthritis were not statistically significantly associated with hospitalization for CTS (table 1). In sex-specific analyses, socioeconomic status, smok-

Table 1. Sex-specific hazard ratios (HR) with 95% confidence intervals (CI) of hospitalization for carpal tunnel syndrome in univariable analysis of total study sample (N=6326). [NA=not available.]

Characteristic	Men				Women				Both genders			
	N	Cases	HR ^a	95% CI	N	Cases	HR ^a	95% CI	N	Cases	HR ^a	95% CI
Gender												
Men	3260	71	NA	NA					3260	71	1	
Women					3066	144	NA	NA	3066	144	2.19	1.65–2.91
Occupational class												
Upper clerical workers	756	3	1		728	19	1		1484	22	1	
Lower clerical workers	653	10	3.87	1.07–14.07	1560	68	1.69	1.02–2.81	2213	78	2.00	1.25–3.22
Entrepreneurs	327	8	6.36	1.69–23.97	155	3	0.73	0.22–2.45	482	11	1.83	0.89–3.78
Farmers, manual workers	1524	50	8.45	2.64–27.09	623	54	3.49	2.07–5.89	2147	104	4.18	2.05–3.76
Body mass index												
Normal	1650	30	1		2152	78	1		3802	108	1	
Overweight/obese	1610	41	1.42	0.89–2.27	914	66	2.06	1.48–2.85	2524	107	1.82	1.39–2.40
Regular smoking												
No	1470	25	1		1775	61	1		3245	86	1	
Yes	1790	46	1.51	0.93–2.46	1291	83	1.92	1.38–2.67	3081	129	1.78	1.36–2.35
Diabetes												
No	3231	70	1		3018	140	1		6249	210	1	
Yes	29	1	1.74	0.24–12.50	48	4	1.86	0.69–5.01	77	5	1.83	0.75–4.44
Thyroid disease												
No	3239	71	NA	NA	2972	137	1		6211	208	1	
Yes	29	0	NA	NA	94	7	1.70	0.79–3.63	115	7	1.53	0.72–3.25
Rheumatoid arthritis												
No	3266	71	NA	NA	3029	142	1		6273	213	1	
Yes	16	0	NA	NA	37	2	1.32	0.33–5.33	53	2	1.08	0.27–4.33
Exposure to heat												
None or light	2645	47	1		2664	114	1		5309	161	1	
Moderate or high	615	24	2.21	1.35–3.62	402	30	1.79	1.20–2.67	1017	54	1.94	1.43–2.65
Exposure to cold												
None or light	2618	50	1		2843	132	1		5461	182	1	
Moderate or high	642	21	1.74	1.05–2.90	223	12	1.17	0.65–2.11	865	33	1.45	0.99–2.12
Exposure to temperature changes												
None or light	1931	32	1		2444	105	1		4375	137	1	
Moderate or high	1329	39	1.77	1.11–2.82	622	39	1.46	1.01–2.11	1951	78	1.57	1.18–2.09
Exposure to vibration												
None or light	2841	45	1		2715	140	1		5858	185	1	
Moderate or high	419	26	3.99	2.46–6.46	315	4	1.87	0.69–5.05	468	30	3.32	2.19–5.03

^a Adjusted for gender (both genders combined)

ing, a BMI of ≥ 25 , self-reported exposure to heat, and temperature changes were associated with CTS among women. Among men, socio-economic status, and self-reported exposure to heat, cold, temperature changes and vibration to hands were associated with CTS, whereas the associations of smoking and a BMI of ≥ 25 with CTS were not statistically significant (table 1).

In the multivariate Cox's proportional hazards regression models, the association of socioeconomic status and CTS remained statistically significant among both men and women and also when both sexes were combined in the analyses. Smoking and obesity were associated with CTS among women and when both sexes were combined. Of the occupational risk factors, only self-reported exposure to vibration to hands was associated with CTS, only among men and when both sexes were combined (table 2).

In the subsample of 3824 participants, physically demanding work at baseline increased the risk of hospitalization for CTS during the follow-up period, whereas lifting < 15 kg, lifting > 15 kg, work requiring arm elevation, and work demanding repetitive movements were not

statistically significantly associated with the incidence of hospitalization for CTS (table 3). In stratified analyses, physically demanding work increased the risk of hospitalization for CTS among overweight or obese participants at baseline, but not among participants of normal weight (supplementary material www.sjweh.fi/show_abstract.php?abstract_id=3835, tables S1 and S2). There were no statistically significant interactions between gender and any personal and occupational variables.

Discussion

In the current study, female gender, overweight or obesity, smoking, and certain socioeconomic classes (lower clerical workers, farmers and manual workers) were risk factors for hospitalization due to CTS. The most important occupational risk factors were exposure to vibration to hands and physically demanding work.

The NFBC1966 is a representative sample of a single-age cohort. The participants are the same age

Table 2. Sex-specific hazard ratios (HR) with 95% confidence intervals (CI) of hospitalization for carpal tunnel syndrome in multivariable analysis in total study sample (N=6326).

Characteristic	Men				Women				Both genders			
	N	Cases	HR ^a	95% CI	N	Cases	HR ^a	95% CI	N	Cases	HR ^a	95% CI
Gender												
Men	3260	71							3260	71	1	
Women					3066	144			3066	144	3.77	2.70–5.25
Occupational class												
Upper clerical workers	756	3	1		728	19	1		1484	22	1	
Lower clerical workers	653	10	3.79	1.04–13.83	1560	68	1.45	0.87–2.43	2213	78	1.74	1.08–2.80
Entrepreneurs	327	8	5.22	1.36–20.03	155	3	0.62	0.18–2.43	482	11	1.48	0.71–3.07
Farmers, manual workers	1524	50	6.15	1.85–20.43	623	54	2.64	1.53–4.55	2147	104	3.02	1.85–4.92
Body mass index												
Normal					2152	78	1		3802	108	1	
Overweight/obese					914	66	1.90	1.37–2.64	2524	107	1.69	1.29–2.22
Regular smoking												
No					1775	61	1		3245	86	1	
Yes					1291	83	1.66	1.19–2.32	3081	129	1.48	1.12–1.96
Exposure to cold												
None or light	2618	50	1									
Moderate or high	642	21	0.93	0.51–1.68								
Exposure to heat												
None or light	2645	47	1		2664	114	1		5309	161	1	
Moderate or high	615	24	1.45	0.84–2.48	402	30	1.32	0.85–2.04	1017	54	1.38	0.99–1.93
Exposure to temperature changes												
None or light	1931	32	1		2444	105	1		4375	137	1	
Moderate or high	1329	39	0.86	0.48–1.52	622	39	1.08	0.72–1.60	1951	78	1.00	0.72–1.37
Exposure to vibration												
None or light	2841	45	1						5858	185	1	
Moderate or high	419	26	2.81	1.63–4.85					468	30	2.29	1.48–3.54

^a Adjusted for all variables in the table**Table 3.** Hazard ratios (HR) with 95% confidence intervals (CI) of hospitalization for carpal tunnel syndrome in multivariable analysis in the sub-sample (N=3824), stratified by body mass index.

Characteristic	Normal weight participants (N=2252)				Overweight or obese participants (N=1572)				All participants (N=3824)			
	N	Cases	HR ^a	95% CI	N	Cases	HR ^a	95% CI	N	Cases	HR ^a	95% CI
Physically demanding work												
No	1283	31	1		789	21	1		2072	52	1	
Yes	969	41	1.34	0.67–2.66	783	51	2.18	1.11–4.29	1752	91	1.71	1.06–2.76
Lifting <15 kg												
No	1005	23	1		578	15	1		1583	38	1	
Yes	1247	48	1.27	0.64–2.53	994	57	1.51	0.74–3.12	2241	105	1.40	0.86–2.61
Lifting >15 kg												
No	1484	40	1		890	35	1		2374	75	1	
Yes	768	31	1.15	0.60–2.23	682	37	0.76	0.42–1.37	1450	68	0.92	0.59–1.42
Work requiring arm elevation												
No	1602	49	1		1060	39	1		2662	88	1	
Yes	650	22	0.74	0.42–1.30	512	33	1.12	0.67–1.87	1162	55	0.94	0.65–1.36
Work demanding repetitive movements												
No	510	10	1		326	6	1		836	16	1	
Yes	1742	61	1.34	0.67–2.69	1246	66	1.80	0.76–4.26	2988	127	1.52	0.89–2.61

^a Adjusted for sex, body mass index, smoking and vibration to hands.

and come from all backgrounds and socioeconomic classes. Their participation in follow-ups has been high. The Care Register of Health Care data are highly reliable and comprehensive, and basically cover the whole healthcare system in Finland. The follow-up time in the presented study is long (mean 18.3 years, SD 4.1 years), and comparable to other published longitudinal studies on CTS (16, 17, 24, 25). During such a long period, it is questionable whether all the exposures remain stable throughout the whole follow-up period.

In this study, the occupational exposures were self-reported and not measured at the workplace. In addition, we had no information on the precise duration of the daily exposure or the number of years exposed. This may have caused misclassification of the exposures. However, CTS has been diagnosed during the follow-up period and its assessment was independent of exposure assessment at baseline.

The socioeconomic status classification includes both occupation and activity in working life (23). In our

study, vibration to hands revealed the most significant occupational exposure, especially among men. Previous prospective studies (17, 26, 27) have reported similar findings. Among women, none of the occupational exposures were associated with CTS in the adjusted analysis, whereas female farmers and manual workers, overweight/obese participants and smokers were at an increased risk. Men and women were divided into socio-economical classes differently; men more often worked as farmers and manual workers and less often as lower clerical workers than women. The occupational exposures differ among men and women; men might encounter more physical risk factors compared to women. The risk factors for CTS may also differ between men and women; occupational exposures being more important among men and personal risk factors among women. However, the current study had low statistical power for sex-specific results. Further larger prospective cohort studies are needed to determine the differences between risk factors for CTS among men and women.

In the subsample analysis, physically demanding work increased the risk of hospitalization for CTS among overweight or obese participants at baseline, but not among normal weight. Obesity may cause CTS through the accumulation of adipose tissue in the carpal tunnel (28). Exposure to physical workload factors may potentiate the adverse effect of obesity through local ischemia-induced reperfusion injury (29).

Although the sample size of the cohort was large (N=6326), the number of participants diagnosed with CTS in the follow-up was quite small (N=215). This might be due to the relatively young age of the cohort, and the registry data we used. As the incidence of CTS has two peaks: 50–59 and 70–79 years (1), the fact that follow-up ended just after the cohort had turned 50 might partially explain the small number of cases. In Finland, public healthcare is divided into primary care (health centers) and hospitals. CTS and suspicion of CTS are coded under the same diagnosis code in the Care Register for Health Care. We only used hospital data because health center data might not be sufficiently reliable. This excludes cases with only mild symptoms and those not willing to consider operations or visiting the hospital polyclinic. All the CTS cases in our cohort were doctor-diagnosed.

To conclude, overweight and exposure to physical workload factors increase the risk of hospitalization for CTS. Being overweight potentiates the adverse effects of strenuous work on CTS. Workplace interventions aimed at reducing excessive workload factors among overweight workers might prevent CTS, but more evidence is needed on this.

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Conflict of interest

The authors declare no conflicts of interest.

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